

# EXHIBIT 12



## ■ ARTHROPLASTY

# Do forced air patient-warming devices disrupt unidirectional downward airflow?

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**Patient warming significantly decreases the risk of surgical site infection. Recently there have been concerns that forced air warming may interfere with unidirectional airflow, potentially posing an increased risk of infection. Our null hypothesis was that forced air and radiant warming devices do not increase the temperature and the number of particles over the surgical site when compared with no warming device. A forced air warming device was compared with a radiant warming device and no warming device as a control. The temperature and number of particles were measured over the surgical site. The theatre was prepared as for a routine lower-limb arthroplasty operation, and the same volunteer was used throughout the study.**

**Forced air warming resulted in a significant mean increase in the temperature (1.1°C vs 0.4°C,  $p < 0.0001$ ) and number of particles (1038.2 vs 274.8,  $p = 0.0087$ ) over the surgical site when compared with radiant warming, which raises concern as bacteria are known to require particles for transport.**

The rate of infection following joint replacement surgery of the lower limb is currently  $< 1\%$ .<sup>1</sup> Both ultra-clean unidirectional airflow and patient warming contribute to reducing the risk of infection.<sup>2-5</sup> However, unidirectional downward airflow is vulnerable to external influences including lights, personnel and equipment. There are also concerns that forced-air warming devices disrupt unidirectional airflow, thus potentially causing a risk of infection.<sup>6</sup>

Ultra-clean unidirectional downward airflow was introduced by Charnley in the 1960s.<sup>7</sup> He reported a reduction in infection following total hip replacement (THR) from 9% to 1%.<sup>7</sup> There is a particular reduction in the rate of infection if it is combined with intravenous antibiotics and sterile occlusive theatre clothing.<sup>8,9</sup>

Whyte et al<sup>2</sup> investigated the use of unidirectional downward airflow and total body exhaust systems. They found that with only plenum ventilation and the use of conventional clothing, the mean airborne concentration of bacterial particles during a THR procedure was 450/m<sup>3</sup>. Using unidirectional downward airflow, but still using conventional clothing, this count was reduced to 7.3/m<sup>3</sup>, a 60-fold reduction.<sup>2</sup> However, when total body exhaust systems were used in conjunction with unidirectional airflow, the bacterial concentration was reduced even further to 0.63/m<sup>3</sup>.<sup>2</sup>

In a multicentre study involving 8052 joint replacements, Lidwell et al<sup>3</sup> concluded that for operations performed within ultraclean air ventilation, the rate of bacterial contamination of the wound, deep joint sepsis, and major wound sepsis were substantially reduced when compared with those operations performed in conventionally ventilated rooms.

Vertical unidirectional airflow ventilation is more effective than horizontal ventilation, especially when combined with walls around the operating area reaching down to 30 cm from the floor, thus extending the unidirectional airflow.<sup>2</sup> Body-exhaust suits have also been shown to further reduce the number of airborne bacteria. Both of these systems are employed in our theatre set-up.

The MRC study in 1984<sup>4</sup> recommended using vertical unidirectional airflow and prophylactic antibiotics to reduce the rate of infection. It showed that the rate of infection fell from 3.4% to 1.7% with the use of ultra clean air alone; to 0.4% when ultra clean air was combined with antibiotics, and to 0.2% through the use of ultra clean air, antibiotics and occlusive clothing.<sup>4</sup>

Bacterial contamination of the air has been shown to be significantly reduced by using ultra clean unidirectional downward air.<sup>2</sup> Our theatre set-up attempts to extend the unidirectional downward airflow and create a barrier between sterile personnel and

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equipment and non-sterile personnel by the use of Howorth enclosure extensions (Howorth Air Technology, Bolton, United Kingdom). Chow and Yang<sup>10</sup> found that as long as unsterile personnel are kept at least one metre from the sterile area, the surgical sites were no cleaner than with conventional air.

In more recent years patient warming has been shown to reduce the risk of surgical site infections, cardiovascular events, peri-operative pain and bleeding by increasing blood flow and tissue oxygen tension in the operative site.<sup>11-13</sup> In addition, maintaining a patient's normothermic core body temperature has been found to decrease the duration of post-anaesthetic recovery and hospital stay.<sup>11-13</sup>

Mild peri-operative reduction in core body temperature is common during major surgery, and may promote wound infection by triggering thermoregulatory vasoconstriction and decreasing subcutaneous oxygen tension. Reduced levels of oxygen in tissue impairs oxidative killing by neutrophils and decreases the strength of the wound healing by reducing collagen deposition.<sup>5</sup> Reduced body temperature also directly impairs immune function, resulting in an increased risk of infection and a prolonged hospital stay.<sup>5</sup>

Kurz, Sessler and Lenhardt<sup>5</sup> undertook a double blinded randomised study into the effects of peri-operative hypothermia, and concluded that intra-operative core temperatures approximately 2°C below normal can triple the incidence of wound infection and prolong hospitalisation by about 20%.

For many years forced air warming has been shown to be an effective method in warming surgical patients undergoing arthroplasty. NICE guidelines state that it is required for patient warming.<sup>14</sup> There has been concern, however, that forced air warming could increase the risk of infection by disrupting unidirectional downward airflow. Also it has been shown that potentially pathogenic organisms can be detected in the hoses of warming devices;<sup>15</sup> however, no such organisms were detected by a study that placed microbial filters over the ends of the hoses.<sup>16</sup>

Sharp, Chesworth and Fern<sup>17</sup> investigated whether forced air warming increased the bacterial level in the operating field. They collected air samples with a slit air sampler, and found no colony forming units (CFUs) on any of the plates exposed inside the unidirectional downward airflow, although two samples taken at floor level had large numbers of CFUs.<sup>17</sup>

To date there have been no papers showing that forced air warming devices disrupt laminar airflow. This study aimed to test our null hypothesis that forced air and radiant warming devices do not increase the number of particles or affect the temperature at the site of the operation, when compared with no warming device.

## Materials and Methods

Two devices were tested against a control (no warming device). The devices used were a torso forced air warming blanket (Bair Hugger; Arizant UK Limited, Wakefield,

**Table 1.** Mean temperature difference over the surgical site with 95% confidence intervals

	Warming device		p-value*
	Forced air	Radiant	
Temperature difference (°C)	1.1 (1.05 to 1.15)	0.4 (0.37 to 0.43)	< 0.0001

\* unpaired *t*-test

United Kingdom) and a radiant warming blanket (Hot-dog, Eden Prairie, Minnesota).

The operating theatre was set up for a routine lower-limb replacement operation in our unit (Northern General Hospital, Sheffield, United Kingdom). A volunteer, who was used throughout the study, was positioned supine on the operating table, without a tourniquet, and draped for a total knee replacement, within an ExFlow 90 Howorth enclosure with vertical wall extensions to 1 metre from the floor. The wall extensions aimed to maximise the unidirectional airflow below the operative site and also to prevent non-sterile theatre personnel from entering the enclosure. The surgeon wore sterile clothing, theatre hood and body exhaust hose. The simulated operation had a single surgeon with no theatre nurse, assistant, or trays within the enclosure and the lights were raised as high as possible, to minimise the disruption of airflow and to identify whether the number of particles or temperature over the surgical site was affected by either of the warming systems. The validation report on the ventilation system conformed to the requirements of the Health Technical Memorandum (HTM) 2025.<sup>18</sup>

Temperature measurements were taken before and 30 minutes after warming using a digital temperature probe positioned 10 cm above the surgical site, and outside the Howorth enclosure as a control to standardise the results. The increase in temperature was calculated by subtracting the temperature after 30 minutes from that before warming, and then standardised using the temperatures recorded during the same period outside the enclosure. This was repeated five times with each warming device (*n* = 5).

The number of particles was measured using a HandiLaz handheld counter (Particle Measuring Systems, Boulder, Colorado) positioned 10 cm over the surgical site, which measured three particle sizes; 0.3 µm, 0.5 µm and 5.0 µm. This was repeated five times. Particle entrainment was calculated as the mean number of particles of each size over the surgical site.

**Statistical analysis.** All the data was evaluated using two-tailed *t*-tests and *p*-values were considered to be statistically significant when less than 0.05.

## Results

The temperature over the surgical site increased significantly when the forced air warming device was used in comparison to the radiant warming device, or control (Table I).

**Table II.** Mean number of particles over the surgical site (CI, confidence interval)

Particle size ( $\mu\text{m}$ )	Mean number of particles (95% CI) [range]			p-value
	Forced air	No warming	Radiant	
0.3	1038.2 (973.1 to 1103.3) [965 to 1150]	274.8 (230 to 310) [193 to 308]	274.8 (231.5 to 318.1) [193 to 308]	0.0087
0.5	30.8 (28.7 to 32.9) [29 to 34]	5.8 (4.2 to 7.4) [4 to 8]	6.8 (5.2 to 8.4) [5 to 9]	0.0073
5.0	3.6 (2.9 to 4.3) [3 to 5]	0.8 (0.4 to 1.2) [0 to 1]	0.8 (0.4 to 1.2) [0 to 1]	0.0038

The number of particles over the surgical site was significantly higher when the force air warming device was used in comparison to the radiant warming device, or control (Table II).

## Discussion

It is our view that both patient warming devices and unidirectional ultra clean downward airflow are needed in lower limb arthroplasty in order to reduce the risk of infection.

Because of the nature of our experiment we are unable to conclude that the use of the forced air warming device, which produced a change in temperature and an increase in the number of particles over the surgical site, would actually lead to an increased risk of surgical site infection. The results do suggest that the downward flow of air is disrupted, as the warming device was lower than at the surgical site.

Forced air warming significantly increased the number of airborne particles over the surgical site compared to the radiant warming or the control, both of which showed similar results. Bacteria require particles to transport them, and although we are unable to confirm if any of the particles were transporting bacteria, the significant increase in the number of particles that we found in this study at the surgical site is of concern.

We have shown that in our experimental theatre set-up forced air warming significantly increases the temperature and number of particles over the surgical site. This may occur via ingress of warm air from the warming device or by direct heating away from the patient, as the warming device creates multidirectional heating in comparison to the radiant warming device which creates unidirectional heating to the patient.

We are therefore able to reject our null hypothesis that forced air and radiant warming devices do not increase the temperature and the number of particles over the surgical site in comparison with no warming device.

Further work is required to confirm that unidirectional airflow is disrupted by forced air patient warming devices under our specific experimental theatre set-up and future studies are needed to visualise the airflow over the surgical site.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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